

WHAT IS CLAIMED IS:

1. A method of identifying two or more latent classes comprising:

(a) providing one or more observations, each of which is associated

5 with at least two members of a plurality of objects, which members can be allocated to at least two or more pre-existing categories; and

(b) estimating one or more properties for latent classes from two or more distinguishable sets of latent classes, to which latent classes members of said plurality of objects may belong, which two or more distinguishable sets of latent classes 10 correspond to two or more pre-existing categories to which members of said plurality of objects can be allocated.

2. The method of claim 1 in which the estimating step of step (b) optionally

further comprises estimating one or more properties of at least one combination of at least 15 two latent classes, which combination comprises at least one latent class from each of at least two of said two or more distinguishable sets of latent classes.

3. The method of claim 1 in which one or more properties of one or more latent classes or combinations thereof are specified and said estimating step of step (b) comprises estimating one or more unspecified properties of any latent classes or combinations thereof.

20 4. The method of claim 1 in which, for at least one latent class in the set of latent classes corresponding to the pre-existing category of one or more members of a plurality of objects, a probability is provided for assignment of said one or more members to said latent class, and said estimating step of step (b) comprises estimating one or more unspecified properties of any latent classes or combinations thereof.

25 5. The method of claim 1 which further comprises:

(c) estimating, sequentially or substantially simultaneously with step (b), for each latent class in the set of latent classes corresponding to the pre-existing category of one or more members of a plurality of objects, a probability that said one or more members belong to said latent class.

5 6. The method of claim 5 which further comprises:

(d) classifying each member of said plurality of objects into one or more latent classes.

7. The method of claim 1 in which the estimating step of step (b) comprises selecting a model appropriate for defining the one or more properties being estimated, 10 which model comprises (i) a specified univariate or multivariate statistical distribution for each latent class and, optionally, for at least one combination of at least two latent classes, and (ii) an appropriate function relating said statistical distributions to said one or more observations.

8. The method of claim 7 in which said one or more observations may 15 include one or more functional transformations of initial observations.

9. The method of claim 7 in which said model can be characterized by a formula:

$$f(\vec{Y}_{j_1, \dots, j_K}) | \left\{ j_k \in S_{km_k} \right\}_{k=1}^K \sim G \left[h \left(k, j_k, \left\{ \left\{ S_{km} \right\}_{m=1}^{M_k} \right\}_{k=1}^K \right) \right]$$

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in which $k \in \{1, \dots, K\}$ provides indexes of various directions in multidimensional space; $j_k \in \{1, \dots, N_k\}$ identifies an object in a direction, k ; N_k represents the number of objects in the direction k ; $\vec{Y}_{j_1, \dots, j_K}$ is a vector representation of one or more observations

on a set of objects, $\{j_1, \dots, j_K\}$; $m \in \{1, \dots, M_k\}$ provides indexes of latent classes in the direction k with M_k being the number of latent classes in the direction k ; S_{km} represents a latent class m in the direction k ; $G[\cdot]$ is a specified univariate or multivariate statistical distribution; and $f(\cdot)$ and $h(\cdot)$ are specified functions, by which one or more parameters 5 are specified for latent classes and, optionally, combinations thereof, which one or more parameters correspond to said one or more properties.

10. The method of claim 9 in which said parameters are estimated by a procedure designed to estimate parameters of statistical distributions.

11. The method of claim 10 in which said procedure comprises a closed form 10 solution, a Bayesian algorithm, an empirical Bayesian algorithm, a frequentist algorithm, a fuzzy set algorithm, or combinations thereof.

12. The method of claim 11 in which said Bayesian algorithm comprises a Metropolis algorithm, a Gibbs algorithm, or a combination thereof

13. The method of claim 11 in which said frequentist algorithm comprises an 15 Expectation Maximization (EM) algorithm.

14. A method of classifying a plurality of objects comprising:

(a) providing one or more observations, each of which is associated with at least two members of a plurality of objects, which members can be allocated to at least two or more pre-existing categories;

20 (b) providing one or more properties which completely specify all latent classes of interest and, optionally, combinations thereof, from two or more distinguishable sets of latent classes, to which latent classes members of said plurality of objects may belong, which two or more distinguishable sets of latent classes correspond

to two or more pre-existing categories to which members of said plurality of objects can be allocated; and

5 (c) estimating for each latent class in the set of latent classes corresponding to the pre-existing category of one or more members of a plurality of objects, a probability that said one or more members belong to said latent class.

15. A computer-implemented method of identifying one or more latent classes, which method comprises:

10 (a) receiving data corresponding to one or more observations or transformations thereof, each of which is associated with at least two members of a plurality of objects, which members can be allocated to at least two or more pre-existing categories;

15 (b) setting a number of latent classes in each of two or more distinguishable sets of latent classes, to which latent classes members of said plurality of objects may belong, which two or more distinguishable sets of latent classes correspond to two or more pre-existing categories to which members of said plurality of objects can be allocated;

20 (c) selecting a model appropriate for defining the one or more properties to be estimated for each latent class, and optionally, combinations thereof, which model comprises (i) one or more parameters for each latent class and, optionally, combinations thereof, which one or more parameters correspond to said one or more properties, (ii) a specified univariate or multivariate statistical distribution for each latent class and, optionally, for at least one combination of at least two latent classes, which statistical distributions employ the said parameters to characterize the distributional properties of each latent class and, optionally, combinations thereof, and (iii) an appropriate function relating said statistical distributions to said one or more observations;

25 (d) estimating the said parameters by one or more procedures, sequentially or in parallel, which procedures are designed to estimate parameters of statistical distributions;

30 (e) diagnosing whether the estimates obtained by application of said one or more procedures are reasonable in the context of the data being analyzed;

(f) altering, as needed, the numbers of latent classes set in step (b) or the model of step (c) and repeating steps (d) and (e) until reasonable estimates are obtained; and

(g) reporting summaries of said parameter estimates.

5 16. The method of claim 15 in which the estimating step of step (d) comprises:

(i) choosing one or more starting values for the parameters of said model; and

(ii) estimating the said parameters by employing the EM algorithm.

10 17. The method of claim 16 which further comprises placing restrictions on the parameters of said model.

18. A method of classifying a plurality of objects comprising the steps of:

(a) providing one or more observations on the objects;

(b) assigning observations as a matrix in a multidimensional space,

15 said matrix having at least two directions for each object of the interest in said space;

(c) identifying latent classes of each object according to a formula:

$$f(\bar{Y}_{j_1, \dots, j_K}) | \{j_k \in S_{km_j}\}_{k=1}^K \sim G \left[h \left(k, j_k, \left\{ \{S_{km}\}_{m=1}^{M_k} \right\}_{k=1}^K \right) \right]; \text{ and}$$

calculating the likelihood that each object of the interest belongs to identified latent classes.

20 19. The method of claim 18 in which $k \in \{1, \dots, K\}$ indexes the directions of the multidimensional space; $j_k \in \{1, \dots, N_k\}$ identifies an object in direction k ; N_k is the number of objects in principal direction k ; $\bar{Y}_{j_1, \dots, j_K}$ is a vector of one or more observations

on a set of objects $\{j_1, \dots, j_K\}$; $m \in \{1, \dots, M_k\}$ indexes latent classes in direction k with M_k being the number of latent classes in direction k ; S_{km} is a latent class m in direction k ; $G[\cdot]$ is a specified an univariate or multivariate distribution; and $f(\cdot)$ and $h(\cdot)$ are specified functions.

5 20. The method of claim 18 in which said objects are classified simultaneously or sequentially.

10 21. A method of identifying one or more genes linked to a cellular phenotype comprising:

15 (a) recording in a matrix one or more measurements on each of the genes subjected to a series of experimental or observational conditions, said measurements forming a first direction in a multidimensional space;

20 (b) providing measurements on a cell or tissue samples subjected to the essentially same series of experimental or observational conditions as in step (a), said measurements forming a second direction;

25 (c) identifying latent classes of the genes in the first direction, and latent classes of cell or tissue samples in the second direction according to formula:

$$\log(Y_{ij}) \mid i \in S_m, j \in G_l \sim N[t_{il} + f(\alpha_{mi}, \beta_{lj}, \gamma_{ml}), \sigma^2], \text{ and}$$

30 (d) calculating the likelihood that each gene is a member of each identified latent class for the first direction, while also calculating, simultaneously or serially, the likelihood that each cell or tissue sample is a member of each identified latent class for the second direction.

35 22. The method of claim 21 in which $N[\cdot]$ refers to a Gaussian distribution; S_m is a latent class m in the first direction; G_l is a latent class l in the second direction; and $f(\alpha_{mi}, \beta_{lj}, \gamma_{ml})$ is a function of the mean parameters of a sample category, gene category, or both.

23. The method of claim 21 in which the cellular phenotype comprises a disease, a cellular process, a physiological pathway, a signaling pathway, a protein expression, a drug effect, or combination thereof.

24. A method of determining in a sample a gene or cluster of genes linked to a disease using a microarray, said microarray including at least one known nucleic acid sequence, an expression and position information, comprising:

- (a) extracting expression and position information to generate a set of data corresponding to at least one dimension;
- (b) assigning in a computer to each dimension of the gene or cluster of genes a numerical value;
- (c) generating in a computer an information algorithm for said extracted information to provide a linking pattern for said gene or cluster of genes; and
- (d) determining whether the gene or cluster of genes in a sample are linked to the disease by extrapolating from the dimension-based numerical values.

15 25. The method of claim 24 in which the information algorithm is constructed in accordance with the formula $\log(Y_{ij}) | i \in S_m, j \in G_l \sim N[t_{il} \cdot f(\alpha_{mt}, \beta_{lj}, \gamma_{ml}), \sigma^2]$, in which i and j are the expression data by gene and sample respectively; m and l are latent classes on the corresponding dimensions; the t refer to gene expression intensity parameters; and various forms for the function f are chosen.

20 26. A method of identifying in a library a gene or set of genes linked to metastatic properties of a cancer comprising the steps of:

- (a) providing a nucleic acid material from a suspected cancerous sample;
- (b) hybridizing the sample-derived probes to the library;
- (c) detecting the differences between hybridization results of the sample and a reference standard;
- (d) recording the differences to form a first set of data;
- (e) analyzing protein expression data to form a second set of data; and
- (f) combining said first set of data and said second set of data to 30 identify the gene or set of genes which govern metastatic properties of the cancer.

27. A method of predicting a metastasizing potential of a cancer, comprising:

- (a) providing a tissue sample from a subject;
- (b) recording predictive parameters, in which the predictive parameters are univariate or multivariate morphometric descriptors; and
- (c) predicting the metastasizing potential of the cancer by a statistical comparison of the recorded predictive parameters with predictive parameters of a reference sample.

28. The method of claim 27 in which the morphometric descriptors are selected from the group comprising optical density, object size, object shape, object color, amount of DNA or RNA, angular second moment, contrast, correlation, difference moment, inverse difference moment, sum average, sum variance, sum entropy, entropy, difference variance, difference entropy, maximal correlation coefficient, coefficient of variation, peak transition probability, diagonal variance, diagonal moment, second diagonal moment, product moment, triangular symmetry, sum entropy, standard deviation, cell classification (1=Hypodiploid, 2=Diploid, 3=S-Phase, 5=Tetraploid, 6=Hyperploid), blobness, perimeter, DNA index, maximum diameter, minimum diameter, elongation, run length, configurable run length and combination thereof.

29. A method of screening for a drug that modulates an expression of a gene or cluster of genes in a cell of interest comprising the steps of:

- (a) exposing said cell to said drug;
- (b) analyzing the gene expression in said cell, and
- (c) comparing by the method of claim 21 the difference in gene expression of a drug-exposed cell to gene expression of a cell not exposed to the drug or exposed to a drug with known properties.

30. A method of identifying a gene or set of genes linked to a disease of interest comprising the steps of:

- (a) registering measured observations of the gene or set of genes as variables associated with said disease at a zero time;
- (b) describing the variables as a matrix in a multidimensional space, in which each variable represents at least one first and least one second dimension in said space;

(c) carrying out, simultaneously or at later times, a series of experimental observations;

(d) determining projections of the experimental observations onto the first and second directions, whereby a multivariate model is obtained;

5 (e) updating during the course of the multivariate analysis at least the first and second directions of the matrix in multidimensional space, whereby the multivariate model provides the likelihood of the gene or set of genes being linked to the disease of interest.

10 31. The method of claim 18 in which said method is used for identifying genes linked to cell or tissue samples collected from a host having or suspected to have a disease comprising the steps of:

15 (a) assigning in a matrix one or more measurements on each of the genes over a series of experimental or observational conditions;

(b) having genes to form a first direction in a multidimensional space;

15 (c) allowing cell or tissue samples collected under differing experimental conditions to form a second direction in a multidimensional space;

(d) identifying latent classes of genes in the first direction and latent classes of cell or tissue samples in the principal direction;

20 (e) calculating the likelihood that each gene is a member of each latent class identified for the first principal direction; and

(f) calculating a likelihood that each cell or tissue sample is a member of each latent class for the second principal direction.

32. A method of classifying a plurality of objects in an image comprising the steps of:

25 (a) inputting at least two distinct images of said objects;

(b) extracting a plurality of characteristics from the images, whereby at least one characteristic of the object in one image is correlated to another characteristic of the object from another image; and

30 (c) generating the classification result according to object membership rules, which represent a relation between the plurality of characteristics and said at least two images.

33. A method of generating membership rules for objects of interest by using a computer, said method comprising the steps of:

(a) placing measurements of a first set of objects into a database of said computer, in which members of said first set of objects, individually, do not necessarily have any hierarchical attributes or characteristics in common;

(b) introducing measurements of a second set of objects into a second database of said computer;

(c) generating the membership rules by including members of said first set of objects and excluding those members of said second set of objects whose individual measurements match with corresponding individual measurements of objects of said first set of objects; and

(d) updating said membership rules by introducing measurements of additional sets of objects and adjusting matching criteria.

34. A method of identifying a gene or set of genes linked to metastatic properties of a tumor comprising the steps of:

(a) providing a sample from suspected tumor;

(b) extracting an experimental genetic data;

(c) detecting the differences between extracted genetic data from the sample and a reference standard; and

(d) generating mathematically an acceptance criteria which allows to link metastatic properties of the cancer to the gene or set of genes.

35. A method of identifying among a plurality of genes of known and unknown function those genes that are linked to a condition of interest, comprising:

(a) providing a mathematical model which utilizes the input data to set rejection margins;

(b) entering an experimental data from the plurality of genes of known and unknown function; and

(c) selecting genes linked to the condition of interest based on an acceptability criteria of the mathematical model.

36. A method of analyzing an image of a plurality of objects arranged as an output signal matrix by comparing to a stored output signal matrix database which sets membership rules for the objects of interest, comprising steps:

- (a) constructing a stimulated physical matrix comprising an ordered array of objects having X and Y coordinates;
- 5 (b) detecting the physical signal at each said object of the physical matrix;
- (c) transforming each said physical signal to generate a corresponding electrical output signal;
- 10 (d) storing each electrical output signal in an output signal matrix database associating each output signal with the X and Y coordinates of the corresponding physical matrix unit; and
- 15 (e) determining the membership of the objects of interest by comparing the output signal matrix database of step (d) with the stored output signal matrix database.